Cell Mol Biol (Noisy-le-grand). 2001 Dec;47(8):1269-75. Related Articles, Links

Gene therapy: some results, many problems to solve.

Fischer A.

INSERM Unit 429, Hjpital Necker-Enfants Malades, Paris, France. fischer@necker.fr

Gene therapy is raising incredible hopes. The prospects of treating numbers of severe pathologies (hereditary, cancerous, degenerative or infectious) are vast. Nevertheless, the technological bolts to lift are still numerous, whether they be bringing the vectors into focus, the systems of expression of transgenes or the neutralization of immune responses of the host against the vector, the product of transgenes, or the knowledge of the considered pathologies of physiopathology. Solving these difficulties entails the gathering of multiple disciplines, from chemistry to medicine, passing through virology and immunology.

Publication Types:
- Review
- Review, Tutorial

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1: Gorecki DC. Related Articles, Links

Prospects and problems of gene therapy: an update.
Expert Opin Emerg Drugs. 2001 Oct;6(2):187-98.
PMID: 15989520 [PubMed]

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Cell Mol Biol (Noisy-le-grand). 2001 Dec;47(8):1269-75. Review.
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☐ 1. 20050123941. 22 Jun 04. 09 Jun 05. Lactobacillus acidophilus nucleic acids encoding fructo-oligosaccharide utilization compounds and uses thereof. Barrangou, Rodolphe, et al. 435/6; 435/200 435/252.3 435/320.1 435/69.1 530/388.26 536/23.2 C12Q001/68 C07H021/04 C12N009/24 C12N015/74.

☐ 2. 20050112612. 23 Apr 04. 26 May 05. Lactobacillus acidophilus nucleic acid sequences encoding cell surface protein homologues and uses therefore. Klaenhammer, Todd R., et al. 435/6; 435/183 435/252.3 435/320.1 435/69.1 530/350 536/23.2 C12Q001/68 C07H021/04 C12P021/06 C12N009/00 C12N001/21 C07K014/335.

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L4: Entry 1 of 1 File: PGPB Mar 20, 2003

DOCUMENT-IDENTIFIER: US 20030054009 A1
TITLE: Clostridium difficile vaccine

CLAIMS:

3. A vaccine as claimed in claim 1 or 2 wherein the gene encodes a C. difficile surface layer protein, SlpA or variant or homologue thereof.

4. A vaccine as claimed in claim 1 or 2 wherein the peptide/polypeptide is a C. difficile surface layer protein, SlpA or variant or homologue thereof.

6. A vaccine as claimed in 5 wherein the chimeric nucleic acid sequence is derived from the 5' end of the gene, encoding the mature N-terminal moiety of SlpA from C. difficile.

8. A vaccine as claimed in 7 wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlPA from C. difficile.

20. A vaccine for the treatment or prophylaxis of C. difficile associated disease, the vaccine comprising the mature N-terminal moiety of a surface layer protein, SlpA of C. difficile or variant or homologue thereof which is immunogenic in humans.

21. A vaccine as claimed in claim 20 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 1.

22. A vaccine as claimed in claim 20 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 2.

40. A chimeric nucleic acid sequence derived from the 5' end of the slpA gene encoding the mature N-terminal moiety of SlpA from C. difficile which is immunogenic in humans.

41. A chimeric peptide/polypeptide wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlpA from C. difficile.

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UniProtKB/Swiss-Prot family/domain classification: SLH (S-layer homology) domain

Family/domain

SLH (S-layer homology) domain

Hierarchical classification

all families and domains
domain
SLH (S-layer homology) domain

CC SIMILARITY line

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CC -!- SIMILARITY: Contains <number> SLH (S-layer homology) domain(s).
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UniProtKB/Swiss-Prot entries and number of domains

SLAP1_CLOTM (Q06852) [4], ANCA_CLOTM (Q06848) [3], APU_THETU (P38536) [
GUN_BACS6 (P19424) [3], SLAP1_BACAN (P49051) [3], SLAP2_BACAN (P94217) [
SLAP2_CLOTM (Q06853) [3], SLAPH_BRECH (P38538) [3], SLAPM_BREBE (P06546) [
SLAP_ACEKI (P22258) [3], SLAP_BACLI (P49052) [3], SLAP_BACSH (P38537) [
XYNX_CLOTM (P38535) [3], Y6545_BACAN (Q9RMZ0) [3], XYNA_THESA (P36917) [
OMPA_THEMA (Q01969) [1], SLAP1_THET8 (Q5SH37) [1], SLAP2_THET8 (P35830) [
Y772_SYNY3 (P15730) [1]

UniProtKB/TrEMBL entry Q9EY85

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Entry information

Entry name	**Q9EY85_CLODI**
Primary accession number	**Q9EY85**
Secondary accession numbers	None
Entered in TrEMBL in	Release 16, March 2001
Sequence was last modified in	Release 16, March 2001
Annotations were last modified in	Release 24, June 2003

Name and origin of the protein

Protein name	**SlpA**
Synonyms	None
Gene name	**Name: slpA**
From	Clostridium difficile [TaxID: 1496]
Taxonomy	Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.

References

[1] NUCLEOTIDE SEQUENCE.
STRAIN=79685;
DOI=10.1128/IAI.69.5.3442-3446.2001; PubMed=11292772 [NCBI, ExPASy, EBI, Israel, Japan]
Karjalainen T.K., Waligora-Dupriet A.J., Cerquetti M., Spigaglia P., Mauri P., Mastrantonio P.;
"Molecular and genomic analysis of two genes encoding surface-anchored proteins from Clostridium difficile.";
Infect. Immun. 69:3442-3446(2001).

Comments

None

Cross-references

EMBL	AY004256; AAF89093.1; -; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
InterPro	~~IPR007253; Cell_wall_bd_2.~~ IPR002035; VWF_A. Graphical view of domain structure.	
Pfam	PF04122; CW_binding_2; 2. Pfam graphical view of domain structure.	
PRINTS	PR00453; VWFADOMAIN.	
ProDom	[Domain structure / List of seq. sharing at least 1 domain]	
HOGENOM	[Family / Alignment / Tree]	

ProtoMap	Q9EY85.
PRESAGE	Q9EY85.
ModBase	Q9EY85.
SWISS-2DPAGE	Get region on 2D PAGE.
UniRef	View cluster of proteins with at least 50% / 90% / 100% identity.

Keywords

None

Features

None

Sequence information

Length: **717 AA** Molecular weight: **76398 Da** CRC64: **52EA6146034FE36B** [This is a checksum on the sequence]

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MSGLTVLASA APVFAADVKA EYITVQKDYK DTLKKIQAGI KDGSITNLVV TYDKDKEVAN

        70         80         90        100        110        120
YNYKSDATTA DAKEIAATTL YNLVDSKLDN LGDGDLVSFN IKYDAAEKFH TKDEMDALKT

       130        140        150        160        170        180
KLENKEIVKP ASETTAGLVM ADGATDSKKA DKSLYAKDVI KFDVVSDTIG YKLTATPIAD

       190        200        210        220        230        240
AQLATLKATY KYANNTKVEF ASATELAATD GSAVEVAKGK EYNATGSLVF DSATGKTSNI

       250        260        270        280        290        300
NVDPLTNKGD TVVKVINAKE STIDIDSSTS TSAEDLAKKY VFDEDKLDDI YKELTSEEGY

       310        320        330        340        350        360
GNLVQLVSGR YQVALYPEGK RLDTKGATDI ENTPVKLVLK ADKIKDMKDY IDDLRTYNNS

       370        380        390        400        410        420
YSNVVTVAGE DRIETAIELS NKYYNSDDKH AITDSATDSV VLVGSQAIVD GLVASPLASE

       430        440        450        460        470        480
KHAPLLLTSK DKLDSNVKSE IKRVMDLKST SGINTSKKVY LAGGVNSISK EVENELKDMG

       490        500        510        520        530        540
LKVTRLSGDD RYETSLAIAD EVGLDNDKAF VVGGTGLADA MSIAPVASQL KKSNGDLDVV

       550        560        570        580        590        600
DGDATPIVVV DGKAKTINNE TEDFLNNAQV DIIGGENSVS KDVEKSIVVA TGKEPNRTSG

       610        620        630        640        650        660
DDRQATNAEV MKETDYFEKG SVINYFVAKD GSTKEDQLVD ALAAAPVAAN FGSTYDGKNA

       670        680        690        700        710
NGTVSPAPIV LATDSLSADQ NVGVSKSVSD DGGKNLVQVG KGIASSVISK MKDLLDM
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Entry information

Entry name	**SLAP2_THET8**
Primary accession number	**P35830**
Secondary accession number	Q6LCW2
Entered in Swiss-Prot in	Release 29, June 1994
Sequence was last modified in	Release 29, June 1994
Annotations were last modified in	Release 49, January 2006

Name and origin of the protein

Protein name	**S-layer protein [Precursor]**
Synonyms	**P100 protein** **Surface layer protein**
Gene name	**Name: slpA** Synonyms: slb
From	Thermus thermophilus (strain HB8 / ATCC 27634 / DSM 579) [TaxID: 300852]
Taxonomy	Bacteria; Deinococcus-Thermus; Deinococci; Thermales; Thermaceae; Thermus.

References

[1] NUCLEOTIDE SEQUENCE [GENOMIC DNA].
PubMed=1429468 [NCBI, ExPASy, EBI, Israel, Japan]
Faraldo M.M., de Pedro M.A., Berenguer J.;
"Sequence of the S-layer gene of Thermus thermophilus HB8 and functionality of its promoter in Escherichia coli.";
J. Bacteriol. 174:7458-7462(1992).

[2] NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 1-11.
PubMed=7476196 [NCBI, ExPASy, EBI, Israel, Japan]
Fernandez-Herrero L.A., Badet-Denisot M.-A., Badet B., Berenguer J.;
"glmS of Thermus thermophilus HB8: an essential gene for cell-wall synthesis identified immediately upstream of the S-layer gene.";
Mol. Microbiol. 17:1-12(1995).

Comments

- ***FUNCTION***: The S-layer is a paracrystalline mono-layered assembly of proteins which coat the surface of bacteria.
- ***SUBUNIT***: Forms trimers in the presence of calcium.
- ***SUBCELLULAR LOCATION***: Cell wall. This bacterium is covered by a S-layer with hexagonal symmetry.
- ***SIMILARITY***: Contains 1 SLH (S-layer homology) domain.

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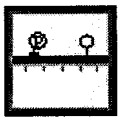
Cross-references

EMBL	X57333; CAA40609.1; -; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	U17352; AAA86987.1; -; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	S26365; S26365.	
InterPro	IPR001119; SLH. Graphical view of domain structure.	
Pfam	PF00395; SLH; 1. Pfam graphical view of domain structure.	
PROSITE	PS01072; SLH_DOMAIN; 1.	
ProDom	[Domain structure / List of seq. sharing at least 1 domain]	
HOGENOM	[Family / Alignment / Tree]	
BLOCKS	P35830.	
ProtoNet	P35830.	
ProtoMap	P35830.	
PRESAGE	P35830.	
DIP	P35830.	
ModBase	P35830.	
SWISS-2DPAGE	Get region on 2D PAGE.	
UniRef	View cluster of proteins with at least 50% / 90% / 100% identity.	

Keywords

Cell wall; S-layer; Signal.

Features

 Feature table viewer

 Feature aligner

Key	From	To	Length	Description	FTId
SIGNAL	1	23	23	*Potential.*	
CHAIN	24	917	894	S-layer protein.	PRO_0000032641
DOMAIN	24	86	63	SLH.	

Sequence information

Length: **917 AA** [This is the length of the unprocessed precursor]

Molecular weight: **96133 Da** [This is the MW of the unprocessed precursor]

CRC64: **16175929CF4CB78F** [This is a checksum on the sequence]

```
        10         20         30         40         50         60
MKKRLVTLLA GLLTVLSMGF GLAQFSDVPA GHWAKEAVEA LAAKGIILGF PDGTFRGNEN

        70         80         90        100        110        120
LTRYQAALLI YRLLQQIEEE LKTQGTSPTM EALAPEDLEA MIAELKAQPM PEPGMDQAAL

       130        140        150        160        170        180
KDLMDRVEAA SIAADTALAQ AQQLAERLDA LAQDVEGVKG DLAGLRSQVE ANADAIQALN

       190        200        210        220        230        240
```

```
ELAVLLNQDV LSLQDRVTAL EKMVSGGQEL PDLEQFATKE DVAAVQEFAA ALRSDLVGLS

       250        260        270        280        290        300
EKVSKLEGTV GDLSGKVATL QRNAFTISGS LSLNYSVYRA WGPDASAAGP GTANTFDIDR

       310        320        330        340        350        360
LFSSKFSTGD GNGNGSVGDE ADLGKNTEGV TNATLSVSFS TGKLDAASDP GKLNSYPGLV

       370        380        390        400        410        420
QFSLRAKLTN PGKYDPSTGA PTYPINLTLD EFSSTLAVAK DQTLSFSFGR SVRSKFTEYV

       430        440        450        460        470        480
FDNDYNSRGH GFVATYKPGL LGATLTGVYG SKGANNGDFT YFRGARLALS PVEGIALGGS

       490        500        510        520        530        540
FVQEGLDANQ GTTSASFPAP TTVYGVDASV KLGPVGLAGE YFNSDAAPNA NGYYVKADVA

       550        560        570        580        590        600
LGSISVAGNY RNIGAGVTGA NMLSGDATST LDQGGWGGVD SSGNVINGAP FRSNRQGFGV

       610        620        630        640        650        660
SASAGLGPIT VKGYYDSSTV LANETITNSY GAFNYSANNQ LVAYGGQADL AFGGFTLSGF

       670        680        690        700        710        720
YRIAQLNGST TRYILTEKPA EAVYASEYGA KLAHDGASKD ALVPKLNFTA AYTQKYDNAT

       730        740        750        760        770        780
SGFTTQDIAV YGSYELALGP LTLKPMGRYH TQDAAAASTS SDYTTVKYGV AASIALDLPF

       790        800        810        820        830        840
KPSLSGEYYA RSTQVTSANS GSSATGTISE SKYAVGLKLG EFLFKNSSVE AKYASYTGSG

       850        860        870        880        890        900
LNAPILLGVA DAASSTTSDY LYNNAVSSVG SNRGSVTGWY FTWTYWDLTF AYVEADVNNN

       910
GNQTHGQAFK ISYTVKF
```

P35830 in FASTA format

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BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Submit a homology modeling request to SWISS-MODEL

NPSA Sequence analysis tools

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L5: Entry 3 of 7 File: EPAB Oct 14, 1999

DOCUMENT-IDENTIFIER: WO 9951631 A1
TITLE: A PROTEIN REGION RESPONSIBLE OF BINDING TO EPITHELIAL CELL TYPES AND A DNA SEQUENCE ENCODING SAID REGION

Abstract Text (1):
CHG DATE=19991102 STATUS=O>This invention relates to a DNA molecule encoding a polypeptide responsible of binding to human and/or animal epithelial cell types. It has been found that various fragments of S-layer protein SlpA of Lactobacillus brevis has adhesive properties to epithelial cells types. It is possible to modify or improve the binding capacity of various prokaryotic or eucaryotic cells to human and/or animal epithelial cell types, like intestinal, urogenital and/or endothelial cell types by using lactobacillar surface structures of this invention. In particular, it is possible with the nucleotide sequences of this invention to improve the binding properties of a host cell having probiotic effects to human and/or animal epithelial cell types.

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